

LABEL AND DRUG

- TWO CRITICAL ESSAYS ON BIOLOGICAL PSYCHIATRY

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ISBN: 978-0-9540761-8-2

PUBLISHED BY

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CLASSIFICATION SYSTEMS: TABLETS IN STONE? A CRITICAL HISTORY OF DSMs

For psychiatrists, the classification systems for mental disorders are the key stone of their profession. Whether it be the American Psychiatric Association's 4th edition of the "Diagnostic and Statistical Manual of Mental Disorders" (DSM-IV; APA 1994) in the USA or the World Health Organisation's 10th revision of the "International Classification of Diseases, Injuries and Causes of Death, Mental Disorder Section" (ICD-10; WHO 1987).

These documents are the basis to the truth of mental illness for psychiatrists. But it must be remembered that mental disorders are constructs; they are not real in the physical sense of objects that can be touched, like a table.

The DSM for most mental health professionals is analogous to the two tablets Moses brought down from Mount Sinai. While the writing on the tablets changes from time to time...the basic categorical and 'externalising' framework remains (Fee 2000 p15).

Their history, and the many changes, suggests that their validity as scientific documents could be open to question. For example, the problems associated with anxiety or nervousness are now classified as "Generalised Anxiety Disorder" in DSM-IV. There are clear criteria for this diagnosis. But the same behaviour was placed under the category "Psychoneurotic Disorder" in DSM-I, "Anxiety Neurosis" and "Phobic Neurosis" in DSM-II, and "Anxiety Disorders" in DSM-III (Kutchins and Kirk 1997).

For Kutchins and Kirk (1997), the history of DSM highlights three themes:

i) The increased "pathologizing" of everyday behaviour;

ii) Linked to this theme is the "pathologizing" of those in society who are undesirable and powerless: "this occurs not because of any malicious intent but because of unspoken cultural biases about what should be considered normal and what should be considered disease" (p16);

iii) And "the fragility of science in the face of political advocacy". "Although the conventional view claims that science and hard evidence underlie decisions about DSM, we find that political negotiation and advocacy - as well as personal interest - are just as, and often more, important in determining whether a mental

disorder is created" (p16).

The origin of all classification systems for mental disorders ⁽¹⁾ is Emil Kraepelin's study of patients in the 19th century. His 6th edition in 1899 reduced thirteen groups of disorders into the big two: affective illness with or without manic depression, or dementia praecox.

Thus by 1899, Kraepelin had elevated the two greater non-organic ('functional') psychoses - manic-depressive illness and schizophrenia - to the top of the pyramid, where they remain in only slightly modified form to this day as the object of endeavour of serious psychiatry (Shorter 1997 p102).

PRE-DSM HISTORY

Psychiatry, particularly in the USA, has always wanted to appear more scientific and be classed alongside medicine. Having clear categories of mental disorder was one such way. Even in the 19th century, behaviours were categorised into melancholia, general paralysis of the insane, and dementia for the annual asylum statistics (Shorter 1997). By 1880, seven categories were used: mania, melancholia, monomania, paresis, dementia, dipsomania, and epilepsy.

1918 saw the first formal set of categories of mental disorder entitled the "Statistical Manual for the Use of Institutions for the Insane". This had been created by committees including the "National Committee for Mental Hygiene". The name of such committees shows the desire of the time to establish what was normal mental health, particularly as a means to control immigration.

In 1933, the "Standard Classified Nomenclature of Disease" was published, which included a section on mental disorders. This document was an attempt to produce a standardised classification of diseases.

Historically, the 2nd World War produced the next challenge to the classification of mental disorders. Many problems appeared that were not common in peace times. From this impetus came, in 1952, DSM-I. The phrase "reaction" appeared throughout, as in "schizophrenic reaction". Many of the terms used were influenced by psychoanalysis which dominated American psychiatry at that time. DSM-I also made the distinction between organic and functional disorders. Functional disorders were then sub-divided into psychosis, psychophysiological, and personality disorders.

FROM DSM-I TO DSM-II

DSM-II appeared in 1968, and was still dominated by psychoanalytic thinking. The term "reaction" was replaced by "neuroses". The very Freudian term "hysteria" replaced "conversion reaction", for example.

Descriptions of all disorders were brief and usually lacking in operational criteria for their application. Psychiatrists seeking guidance in differentiating, for example, schizophrenia from mania would find little to help them (Shorter 1997 p300).

The main categories in this version of DSM were "organic brain syndromes", psychoses and neuroses, psychophysiological, special syndromes, transient states, and mental retardation.

FROM DSM-II TO DSM-III

The pressure to change DSM-II came from a number of directions. One was the need to have operational criteria for the disorders. Another was dissatisfaction with the dominance of psychoanalysis.

Also there was concern about homosexuality being included as a disorder. The removal of homosexuality as a disorder, or more correctly, the removal of the wording (2) is the largest political consideration in the history of DSM (Kutchins and Kirk 1997). DSM-III was published in 1980.

The Task Force within the American Psychiatric Association that produced DSM-III had, for the first time, a predominance of biological psychiatrists over psychoanalysts. The biological psychiatrists encouraged the field trials of the new categories before publication. Between 1977 and 1979, 500 psychiatrists were involved.

DSM-III now contained 500 pages, whereas DSM-II only had 134, was called a "victory for science" (Shorter 1997). The medical model had come to control psychiatry in the USA (3). More than that, DSM-III was seen as a "signal achievement for psychiatry" in indicating a "professional consensus" in diagnosis (Bayer and Spitzer 1985).

Gaines (1992) feels that a major change has occurred:

In terms of diagnosis, the identification of symptoms is transformed from an interpretation of symbols of

distress into a reading of signs of disease. No longer would clinicians gaze upon symptoms as symbols of psychosocial, intrapsychic conflicts... (p9).

Kirk and Kutchins (1992) call this a "palace revolt", and show the individual politics behind the committees that produced DSM-III.

DSM-III was multi-axial in its diagnosis. This is the basis of the classification system today. The diagnosis of the mental disorder is one of five diagnoses. The five axis are:

- Axis I - clinical syndromes (patient's specific psychological disorder at the time of diagnosis);
- Axis II - developmental disorders, personality disorders;
- Axis III - Physical disorders and conditions (eg: low blood sugar level);
- Axis IV - severity of psychosocial stressors (scale 1-7; "none" to "catastrophic");
- Axis V - global assessment of functioning (in past year) (scale 1-100; "extreme" to "superior functioning in range of activities"); this was expanded in DSM-IIIR.

Whether this was a victory for science or not, the number of categories of mental disorder kept growing. DSM-II had 180 discrete disorders, DSM-III 265, DSM-IIIR (1987) ⁽⁴⁾ 292, and DSM-IV (1994) has 297 categories (Shorter 1997). "Yet the sheer endlessness of the syndrome parade caused an uneasy feeling that the process might somehow be out of control" (Shorter 1997 p303).

But Stone (1998) believes that "Despite their imperfections DSM III and IIIR represent a laudable attempt to bring global unity to the field of psychiatric diagnosis" (p302).

POLITICS OF DSM

DSM-III was criticised primarily for being "too American"; ie: some disorders, like anorexia nervosa, were unknown in some parts of the world.

If supposedly scientific psychiatry was merely trying to classify the cultural preoccupations of the North American middle class, its naming manuals would soon be as outdated as the etiquette guides

for Victorian ladies (Shorter 1997 p303).

The dominance of "Northern European Germanic Protestant" values (Gaines 1992).

The construction of DSMs has always involved politics, and this can be seen in the inclusion of post-traumatic stress disorder (PTSD) in DSM-III. Called many terms beforehand, the experiences of returning USA Vietnam veterans were a challenge to older terms like "soldier's heart" or "battle fatigue".

Summerfield (2001) is clear about the origins of PTSD:

Vietnam veterans were to be seen not as perpetrators or offenders but as people traumatised by roles thrust on them by the US military. Post-traumatic stress disorder legitimised their 'victimhood', gave them moral exculpation, and guaranteed them a disability pension because the diagnosis could be attested to by a doctor (p95).

Young (1995) adds:

The disorder is not timeless, nor does it possess an intrinsic unity. Rather, it is glued together by the practices, technologies and narratives with which it is diagnosed, studied, treated, and represented and by the various interests, institutions, and moral arguments that mobilised these efforts and resources" (quoted in Summerfield 2001 p97).

It is interesting to note that the criteria for diagnosing PTSD included eleven changes in DSM-III-R, and fifteen more in DSM-IV.

Ziskin (1995) notes 175 combinations of symptoms by which to diagnose PTSD, and also that it is possible to have or not have PTSD depending on the edition of DSM (even if the individual's symptoms remain unchanged).

Robert Spitzer (5), the editor and chair of DSM-III, admitted the influence of political considerations. For example, the pressure from feminist groups to remove "paraphilic coercive disorder" (rape) from DSM-III-R; "masochistic personality disorder" changed to "self-defeating personality disorder" and placed in the appendices as "needing further study". This was then removed in DSM-IV "so as not to stigmatise women".

Some categories, fortunately, do not make it to DSM itself. Robert Spitzer proposed a diagnostic category of

"Victimization Disorder". For example, it was for those who experience abuse or witness violent crime. The criteria for diagnosis contained thirteen items which combined to account for the victim's "distorted view" of the self, the experience, and the world. The diagnostic criteria included "exaggeration of the powers of the perpetrator" and "lack of believing that authority figures will come to one's help even when help is clearly available" (quoted in Kutchins and Kirk 1997).

TODAY: DSM-IV

Including the appendices, there are 330 categories of mental disorder in DSM-IV (published in 1994) (Stone 1998). "Organic mental disorder" is a term which has been dropped. While the new term "dysfunction" became commonly used, but, for Carson (1997), it is never defined.

Kutchins and Kirk (1997) are critical of the growth in categories, including the suggestions of future disorders that need further study, but will probably appear in DSM-V. The authors give the example of motorists who drive above the speed limit, which could be included as "Excessive Motorised Speed Disorder".

For Kutchins and Kirk (1997), DSM has become "a guidebook that tells us how we should think about manifestations of sadness and anxiety, sexual activities, alcohol and substance abuse, and many other behaviours" (p11).

FOOTNOTES

(1) The term "mental disorder" is not used until the later versions of DSM, but it is the common term used today in psychiatry.

DSM-IIIR defines mental disorder as: "A clinically significant behaviour or psychological syndrome or pattern that occurs in a person and that is associated with present distress (a painful symptom) or disability (impairment of one or more important areas of functioning) or with a significantly increased risk of suffering death, pain, disability, or an important loss of freedom. In addition, this syndrome or pattern must not be merely an expectable response to a particular event, for example, the death of a loved one".

(2) In DSM-II, homosexuality was named as a classification under "sexual deviations". While in DSM-III, "ego-dystonic homosexuality" (EDH) was used: "a sustained pattern of overt homosexual arousal that the individual explicitly states has been unwanted and a

persistent source of distress" (p282). This category was dropped in DSM-IIIR.

Now in DSM-IV, there is "sexual disorders not otherwise specified" for "persistent and marked distress about sexual orientation" (p538). Kutchins and Kirk (1997) point out that "psychiatrists have seemingly agreed not to call their clients homosexual, although they have indirect ways of identifying homosexuality" (p91).

(3) "DSM-I and DSM-II made no pretence to being scientific documents. They were administrative codebooks put out by a small obscure committee" (Kutchins and Kirk 1997 p24).

(4) DSM-IIIR was published "in order to solve a number of technical inconsistencies in DSM-III" (Frances et al 1996).

(5) Kirk and Kutchins (1992) see Spitzer as a key figure in the history of DSM, and particularly in the changes that came with DSM-III.

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CHLORPROMAZINE - NEARLY 50 YEARS OLD: SHOULD IT HAVE MADE IT THIS FAR?

The number of prescriptions of neuroleptics (NLP) generally, and of chlorpromazine (CPZ) specifically, is immeasurable. Estimates suggest tens of millions in nearly 50 years. This is not just for individuals suffering from psychotic disorders (primarily schizophrenia), but also for nursing home residents, and those with developmental or learning disabilities (Ray et al 1993). Ironically, though, NLPs are less prescribed than other psychotropic drugs.

From the patient or client's viewpoint ⁽¹⁾, they do not necessarily request NLPs, nor like them. The obvious reason being the level of side effects or, in the jargon, iatrogenic morbidity: eg: tardive dyskinesia or neuroleptic malignant syndrome (which can be fatal).

Nevertheless, most clinicians today consider NLPs indispensable to treat psychotic disorders and it is very likely that a person diagnosed with schizophrenia will receive these drugs for months, years, or indefinitely (Cohen 1997 p174).

This general support by clinicians is often a matter of creed than of scientific evidence.

Julien (1995), in the commonly used "A Primer of Drug Action" admits:

Indeed, much of the art of managing patients with schizophrenia is in the diagnosis and management of the side effects of neuroleptics. One chooses one drug over another not so much because of differences in therapeutic efficacy but because of the relative intensities of their side effects (p285).

When evidence is provided against the use of NLPs, it is marginalised by arguments about controlling "dangerous mental patients", or the lack of effective non-drug alternatives, or the humaneness of using drugs to alleviate suffering. It is possible to remain so close-minded about the use of NLPs that we are only a short step away from blaming the victim for the side effects and the lack of efficacy of the drugs.

Occasionally, clinicians question NLPs' all powerful use. For example, Pierre Deniker, one of the "founders" of CPZ use, in a 1986 article; though he did not reject their use.

This essay argues that the serious side effects of CPZ (and NLPs) have always been seen as a "necessary evil" because the drugs help people. But this latter point is open to debate, which means that iatrogenic effects are seen as a "normal" part of mental illness.

HISTORY

The drug itself was synthesized by Rhone Poulenc in December 1950, and marketed in the USA as "Thorazine" by Smith, Kline and French, and as "Largactil" by May and Baker in England. CPZ is a phenothiazine derivation, and this group of drugs had been used since the late 19th century to treat parasite worm infections in animals.

Anti-histamines also have a phenothiazine nucleus (2), and they had been used in the 1940s for surgery shock, particularly by French surgeon, Laborit. Other French surgeons, including Huguenard and Alluaume, were using them for their anaesthetic properties (3).

Charpentier, a French chemist, prepared the phenothiazine derivative, originally called 4560 R-P, for its use in surgery to slow the pulse and heart rates. In the USA, the original interest in CPZ was as a treatment for itching and to control nausea. Thus its use in psychiatry is almost an afterthought.

Swazey (1974) is particularly critical of the frantic attempt to convince the Food and Drug Administration (FDA) in the USA for a licence, and to persuade US doctors to use it. By the end of 1953, only 104 patients had been tested. It was licensed in the USA in 1954, and within a year, two million patients were taking CPZ.

The power of the pharmaceutical companies can be seen in the decision in 1954 by Smith, Kline and French to employ 50 salesman just for "Largactil", out of a total sales force of 300. Does this account for the sudden uptake of the drug in the USA?

The "founders" of CPZ use in psychiatry are seen as the French psychiatrists, Jean Delay and Pierre Deniker at St.Anne Hospital, Paris, in May 1952. They used it with six patients initially, then another 32.

Technically, CPZ had been used alone in the form of an experiment in 1951. Leon Chertok injected, with consent, an unspecified amount of CPZ into psychiatrist, Cornelia Quarti, whose comments during the experience were recorded (Chertok 1982).

Shorter (1997) argues that "Jacques L" (suffering from mania) was the first psychiatric use in the French hospital of Val-de-Grace in January 1952 (4).

The first British report of CPZ use, by Anton-Stephens (1954), identified indifference as the greatest effect on the patients. This observation was linked to the similar response shown to psychosurgery ("frontal lobe syndrome"), which was quite popular at the time; again with little clear scientific support. The phrase "chemical lobotomy" was used by the early authors (eg: Lehmann 1989).

Shorter (1997) quotes a member of Smith Kline:

What this drug did was not to cure these patients but to trip the balance enough so that the doctor and the nurse in the hospital said, 'Hey, maybe we can do something for these people'.

At the same time, the early authors were aware of the "parkinsonian" side effects (Letailleur et al 1956). Steck (1954) first formally noted these side effects in around one third of 300 patients. The symptoms were called "basal ganglia dysfunction". While at a New York Hospital, the figure was "probably two-thirds" (quoted in Cohen 1997). Similarly these side effects were noted in Germany (Haase 1958).

In 1957, the term "neuroleptics" (meaning "takes hold of the nerve") was coined to define CPZ and related compounds (Delay and Deniker 1961). The five characteristics of CPZ are shown in Table 1.

Cause "psychic indifference"
Have sedentary effects
Reduce psychotic disorder
Produce extra-pyramidal side effects
Have sub-cortical effects

Table 1 - Five characteristics of CPZ and related compounds.

Thus the psychiatrists first using CPZ were clearly aware of the powerful side effects, which it was believed were part of the therapeutic effect. In fact, some argued that deliberate production of the "basal ganglia dysfunction" may be desirable.

This belief has to be seen in the context of psychiatry in the first half of the 20th century.

Very few methods used to treat patients had scientific evidence to support their use, let alone efficacy. For example, in the 1940s, the treatments available included insulin-induced coma, electro-convulsive therapy (without muscle relaxants),

"carbon dioxide treatment", "very large doses of caffeine", and injections of sulphur in oil and typhoid anti-toxin (Lehmann 1989).

These examples illustrate "the notion that, in devising experiments for their forgotten and socially devalued wards, asylum doctors had little incentive to choose treatments causing least harm" (Cohen 1997 p179).

How many patients in mental institutions in the first half of the 20th century died from these experiments? It is impossible to know. But for psychiatrists, not necessarily because they were malevolent, treatments without harm or side effects were unknown. The pain of the treatment is less than the pain of the illness, they argued. Working within a mentality that accepts pain in treatment means that unpleasant side effects are dismissed as a "necessary evil". Thus this attitude remained even with the introduction of psychotropic drugs, and probably still does today.

Cohen (1997) argues that early writers on CPZ had "a blind spot about NLP toxicity". These clinicians simply saw a parallel between NLP and encephalitis lethargica (EL). Again it was not unknown for psychiatrists to try and produce one disease in order to cure another. For example, malaria therapy was tried by psychiatrists in the early 20th century as a treatment for serious mental illness.

However, what the psychiatrists saw in the similarity between NLP and EL was evidence that there were clear biological causes for mental disorders (Cohen 1997).

CPZ USE TODAY

The attitude of clinicians today is that the side effects of CPZ are inevitable, and an unpleasant part of getting better. A bit like the horrible taste of the medicine to the little child. They are given sweets afterwards to remove the taste. Today patients receiving NLPs are given other drugs to reduce the side effects. This can produce a very extensive drug regimen each day. I am sure that the pharmaceutical companies are not unhappy about this fact.

Examination of CPZ and NLP use today identifies two key questions, which are often overlooked, or assumed unnecessary to answer - what is the appropriate dose, and do the drugs actually "work"? After nearly 50 years of CPZ use, surely these basic questions have been answered?

DOSE

CPZ, based on an oral dose, appears in the blood 30 minutes after swallowing, and reaches a peak concentration in three hours (Green 1994).

The "correct" or appropriate dose of a drug will be recommended by the drug manufacturers. This will be based upon trials with animals and humans to establish the "minimum effective dosage", and the "maximum tolerated adverse effects" ⁽⁵⁾. The difference between these two points is known as the "therapeutic range".

Though there are recommended dosages, there is no definitive decision on how much is best. This can vary between studies, and the "judgement" of the clinicians. The "Nurse Prescribers' Formulary" (BMA 1999) recommends, for oral doses, initially 25mg three times daily, and an usual maintenance dose of 75-300mg daily. While Reid et al (1996) suggest: "orally 100mg daily, increasing up to 1g gradually if required" (p282).

In an Austrian study, Meise et al (1994) found that the recommended dose of NLPs could vary from 40mg/day to 2000mg/day CPZ equivalents.

Minimum effective NLP dosages have not yet been determined, nor have investigators been able to demonstrate, even with the most sophisticated fixed-level blood studies, the existence of therapeutic plasma levels of NLPs (Cohen 1997 p188).

In the USA, in particular, the doses are traditionally higher as there is a pressure "to do more and to do it faster" (McIntyre and Simpson 1995). USA doses have always been higher than in Europe: "American psychiatrists were more hurried than their European colleagues" (Deniker 1990).

In fact, "ingrained practice habit" seems to be what matters:

treatment zeitgeist may actively bias clinicians in favour of NLPs, influencing them to disregard essential information with critical bearing on their own prescribing behaviour, their patients' clinical outcomes, and their judgment on the overall value of NLPs (Cohen 1997 pp189-90).

EFFICACY/EFFECTIVENESS

It may be acceptable to experience unpleasant side effects if the drugs worked. "Efficacy" of the drug means the outcomes under ideal conditions, while

"effectiveness" is how well it works under practice conditions (Zito and Provenzano 1995). The former involves controlled environments, and compliant and homogeneous patients. For the latter, it can be the complete opposite. Thus studies do report different figures for these reasons.

The main focus of evaluation of drug treatment is to compare the chosen drug to a placebo in a random-assigned, double-blind study. In particular, the patients or the staff administering the drug do not know who is the placebo group.

An early study of CPZ occurred in France in 1959 (Follin et al 1961). There are ethical concerns about repeating this study today because the psychiatrist covertly replaced CPZ with a placebo in a certain number of patients over a nine month period.

There was no evidence of any change in behaviour compared to when CPZ was being given. This finding highlights the general problem of drug trials - placebos do have an affect themselves, rather than being a baseline by which to compare the active drugs.

Such studies are faced with a number of technical problems - the most prominent being how to define "works". By common agreement it is usually based on relapse in a certain time period. But definitions of relapse can vary.

There are many studies of NLPs generally. Keck et al (1989) estimates 1300 between the mid-1950s and late 1980s. The general picture is that NLPs produce less relapse than placebo. Or more correctly: for those patients who do not relapse in a set time period, NLP treatment seems to be the determining factor.

In a more recent meta-analysis of 42 studies of CPZ compared to a placebo or no treatment for schizophrenics, Thornley, Adams and Awad (1997) found that less patients on CPZ relapsed after 2 or 5 years. The relapse rates for CPZ were 40% at 2 years and 55% at 5 years. For the control group, the figures were 71% and 83% respectively. In terms of improvement in the short term, 30% of the CPZ group at 6 months compared to 13% in the control group.

However, there was no escaping the side effects: 41% of the CPZ group experienced weight gain, 28% sedation, 20% eye problems, and 6% dystonia. These categories may overlap; ie: the same person may suffer from a number of side effects. There is no record that those who did not relapse or who improved experienced the side effects only. In other words, the price of the side effects was worth it. There must have been some patients who experienced side effects without any benefits.

But very few of the studies assess "quality of life"

for the patients (Cohen 1997). This dimension is far too subjective, and without a clear definition, it is argued.

This disregard for schizophrenic patients' accounts of their subjective experience is based on the notion that these accounts are unreal since patients suffer from disturbed thinking and communication (Cohen 1997 p193).

It is better to use "objective" or scientific data instead. This is what we are led to believe, yet data is interpreted in a subjective way; ie: to support the effectiveness of NLPs. Cohen (1997) quotes examples of studies where the data has been "polished"; ie: certain categories changed or excluded in the statistical analysis.

The overall usefulness of NLPs in the treatment of schizophrenia - conceived as a broad, episodic impairment of various social-interpersonal-cognitive abilities - is far from established (p195).

Other issues related to the effectiveness of NLPs include:

i) Non-response to treatment

Often this issue is avoided in the literature. Crow (1989) was the first to note that different types of schizophrenia responded differently to drug treatment. Type I schizophrenia tends to respond to drug treatment, whereas type II does not ⁽⁶⁾. Newer drugs have challenged this distinction (Green 1996).

But for Cohen (1997), "one senses that non-response is quite common". The figure may be as high as 50% (Collins et al 1992; Canadian study), if not higher.

If the phenomena of non-response is accepted, this has serious implications for the use of drug treatments, and for psychiatry as a whole. What would psychiatrists do if they had to admit that their ability to treat severe mental disorders was limited.

The introduction of psychotropic drugs since the 1950s has made many improvements compared to the limited effectiveness of earlier treatments. But what if the ability to treat today was not that much better in some cases? There is a lot at stake for psychiatry.

Caldwell (1970) quotes the "official view" of CPZ at in the early days:

By May (1953), the atmosphere in the disturbed wards of the mental hospital in Paris was transformed. Physical restraints were a thing of the past! (p72).

However, Johnstone (2000) challenges the belief that CPZ, among other drugs, led to a decline in long stay patients in mental institutions, and to the revolution in psychiatry that is claimed. She argues that the arrival of the new psychotropic drugs coincided with a move to reduce asylum populations, through, for example, the Open Door Movement.

ii) Withdrawal

One way to test the effectiveness of NLPs is to stop the drugs and see what happens. In a number of studies, the cessation of the drug is abrupt, and not surprisingly, problems occur. Where there is gradual withdrawal, relapse is not inevitable (Cohen 1997).

iii) Lack of non-drug alternatives

Traditionally psychiatrists have argued that NLPs are necessary because of the severity of psychotic disorders, and that there are no effective non-drug alternatives. This is again wishful thinking on the part of psychiatry.

A small number of studies of "therapeutic communities" show effective results for schizophrenic patients; eg: Soteria, California (Matthews et al 1979) and Switzerland (Ciompi et al 1992). These communities can be effective with minimum doses of NLP or none at all. Relative to drug prices, treatment costs of these communities are high. The old issue of money versus patients.

SIDE EFFECTS

There is no denying the side effects of NLPs, nor their intensity. But, as psychiatry argues, the side effects are seen as a "necessary evil" because of the effectiveness of the drugs. This proposition is certainly open to question.

In fact, Heinz Lehmann making early use of CPZ in Canada, in 1953, noted that the patients "walked with a peculiarly stiff gait" and had "that peculiar mask-like face" (quoted in Shorter 1997). But Lehmann was too excited by the disappearance of the symptoms of schizophrenia in a matter of weeks to pay too much

attention to these "innocuous side effects".

Pathare and Paton (1997), in assessing the potency of different NLPs in relation to their side effects, see CPZ as low potency with high anti-cholinergic and sedative side effects. Anti-cholinergic side effects include dry mouth, blurred vision, and constipation.

The most serious side effects are known as extra-pyramidal side effects (EPSE), which include parkinsonism, dystonia, akathisia, and tardive dyskinesia. Disturbingly, EPSE may be irreversible, even after cessation of the drugs.

It is distressing that the side effects of tardive dyskinesia could continue after the cessation of the drug. Because CPZ has blocked the dopamine receptors in the brain, the neurons there manufacture more receptors. Thus when the drug is stopped, these new receptors still exist and tardive dyskinesia continues. This is known as the "upregulation" of dopamine receptors (Marland and McSherry 1998).

Tables 2 and 3 gives the main details of EPSE.

Even the "Oxford Textbook of Psychiatry" (Gelder et al 1989) is aware of the seriousness of these side effects, and sees them as "a deterrence to the long term prescribing of antipsychotic drugs in large doses" (quoted in Gross 1992 p965).

Parkinsonism

- this includes reduced facial expression, general muscular rigidity, monotonous speech, tremors and uncontrollable shaking of the limbs, and excessive salivation.

Dystonia

- including unco-ordinated movements, forced opening of the mouth, tongue protrusions, and swallowing difficulties.

Akathisia

- including inability to sit still, shifting weight from foot to foot when standing, and inability to keep legs still.

Tardive dyskinesia

- has up to 25 different symptoms including movements and grimaces of the mouth, and tics and mannerisms.

Table 2 - Details of extra-pyramidal side effects

SYMPTOM	PREVALENCE	COMMENTS
parkinsonism	30% (Van Putten and May 1978)	gradually disappears after few months on drugs; can persist after drug cessation
dystonia	1-10% (Dewan and Koss 1989)	younger, male patients particularly predisposed
akathisia	5-76% (Cohen 1997)	resistant to other drugs to remove it; persists after drug cessation
tardive	38% after 5 years; 56% after 10 years; (Bezchlibnyk-Butler and Jeffries 1996)	spontaneous remission 14-40% after 5 years without drug

Table 3 - Prevalence of extra-pyramidal side effects

The acceptability and normality of side effects can be seen in the drug company's official data sheets for pharmacists. The official data sheet for "Largactil" preparations lists twenty-one possible side effects, varying from nasal stuffiness to neuroleptic malignant syndrome (ABPI 1999). While the respected "Martindale Complete Drug Reference" (Parfitt 1999) gives details of research showing adverse effects on twelve areas of physiology (details in table 4). Though dependence is not encountered, Parfitt argues, withdrawal symptoms have been seen.

While Holmes (1997), in a typical medical textbook, lists twenty "side effects and idiosyncratic reactions" which "may be produced" with NLPs.

The side effects are unpleasant in themselves, but what about the experiences of the sufferers? Rifkin et al (1975) report the case of a young man who suffered depression and suicidal thoughts because he could not hold conversations and interact socially due to the side effects. The patient is suffering from psychological problems with their disorder and the social stigma of that disorder, the physical side effects of the medication, and, on top of that, changing appearance and accentuated social distance (Diamond 1985). Is it surprising that patients show depression and suicidal thoughts?

As it stands at the moment, the NLPs used will produce unpleasant side effects because of their biochemical nature; eg: working on dopamine synapses. But it is psychiatrists' resistance to change that exacerbates the problem - a resistance to inform patients about EPSE, a resistance to changing prescription habits, and a resistance to acknowledge the negative side of NLPs (Cohen 1997).

AREA OF PHYSIOLOGY	EXAMPLE OF EFFECT	LEVEL OF OCCURRENCE
1. Convulsions	lowered seizure threshold	less than 1% risk
2. Blood	agranulocytosis (change in white blood cells)	51 reports with 26 fatalities between July 1963-Jan 1993
3. Cardiovascular system	orthostatic hypotension (drop in blood pressure on standing)	common
4. Endocrine function	secretion of prolactin (involved in lactation)	short and long term effects
5. Eyes	pigmentary retinopathy (eye problems)	"relatively few cases"
6. Fluid and electrolyte homeostasis (balance of fluid intake and excretion)	hyponatraemia (low sodium levels)(7)	"unclear"
7. Lipid metabolism (conversion of fats into energy)	elevated cholesterol levels (and consequent risk of heart problems)	only for patients with risk beforehand
8. Liver	hepatocanalicular cholestasis (imbalance in liver functions)	small number of
9. Sexual function	male sexual dysfunction eg: inhibition of ejaculation (Holmes 1997)	around quarter of patients
10. Skin	chronic reactions to injections	common in patients aged over 50 years
11. Extra-pyramidal effects	parkinsonism	"major problem"
12. Neuroleptic Malignant Syndrome (fever, muscular rigidity, coma and death)	fatal reaction	0.02-2.5%

Table 4 - Areas of physiology affected by CPZ as listed in "Martindale Complete Drug Reference" (source: Parfitt 1999).

Around half of the respondents in a USA study of state psychiatrist admitted to not disclosing the risks of EPSE to patients (Kennedy and Sanborn 1992).

Cohen (1997) says that he:

looks in vain across the medical literature for...prominently titled cautions advising physicians to inform patients and families of the prevalence of a vastly more compelling case, that the emergence of movement disorders with the progression of NLP treatment (p212).

PRESCRIBING CPZ AND NLPS

Despite the well-established unpleasant side effects of CPZ and NLPs generally, their prescribed use continues in abundance. Two key issues about their use concern many individuals: the appropriateness of prescribing them, and the major health risks attached to their use.

i) Appropriateness of prescribing

Whether CPZ and NLPs help individuals suffering from psychotic disorders is another question, but their use is with many other groups, like residents of nursing homes who have no major mental disorders.

In a recent study in south Glasgow, McGrath and Jackson (1996) investigated 28 nursing homes with 909 residents, of which 217 were prescribed NLPs (20 of these were CPZ). The authors applied US criteria, which state that NLPs are only appropriate for psychotic disorders, or organic disorders with danger to others or interference with caring. Under these criteria, only 12% of the residents were receiving NLPs appropriately.

For older people, long term use of NLPs produces increased risks of hip fractures, and constipation, and impaired cognitive functions as specific side effects.

ii) Major health risks

On top of the general side effects of NLPs, there are some concerns about serious health risks of their use, including possible death.

For example, a Canadian study of asthma sufferers taking NLPs had a 3.2 times greater risk of death or near death from an asthma attack.

Based on a study of 131 cases, the researchers found that those who has recently discontinued NLPs had a relative risk of 6.6 of the same problem (Joseph et al 1996).

It is always difficult to know whether NLPs are directly the cause of death. But there is the case of "sudden unexpected death" (ie: within one hour of the symptoms appearing), and it cannot be explained by illness or autopsy.

Jusic and Lader (1994) reviewed eight such cases, and noted that five of them had toxic concentrations of NLPs or anti-depressants, which probably caused cardiac arrhythmias. The cases were not overdose victims - accidental or deliberate.

CONCLUSION

CPZ, and NLPs generally, are not pleasant for those who take them. This may be acceptable if there was clear evidence of their efficacy. It is a question of psychiatrists giving the facts to the patients and their families. As with many techniques within psychiatry, now and in the past, CPZ's continued use is just because.

FOOTNOTES

(1) The terms "patient" or "client" themselves show the attitude of the psychiatrist or therapist to the individual they are working with. Traditionally in biological psychiatry, the term "patient" is used.

(2) The German chemist, August Bernthsen, synthesized phenothiazine in 1883. It is a chemical produced by a combination of other elements; ie: it is not naturally occurring. The chemical formula, Bernthsen reported, was $C_{12}H_9N_5$ (Swazey 1974).

(3) Swazey (1974) outlines the complete history of the synthesis of CPZ from the origins of synthetic organic chemistry with the dye industry in the 19th century.

(4) As to which study was chronologically the first to use CPZ, there is some debate. Shorter (1997) points out that Sigwald and Bouttier began a study on 48 patients on 18th February 1952, but did not publish the results until 1953.

However, Cunningham Owens (1996) prefers the date of "28 Dec 1951, J.Sigwald started solo CPZ treatment of a 57 year-old psychotic lady" as the beginning of the "modern era of psychopharmacology" (p556).

(5) "Minimum effective dosage" is where the drug first has a positive effect on the body. The "maximum tolerated adverse effects" is where the side effects become greater than the positive effects. These figures are calculated statistically, and are not necessarily based on the views of the takers of the drugs.

"The difference between the concentration that produces the desired effect and that which causes adverse effects is called the therapeutic index and is a measure

of a drug" (Reid et al 1996 p6).

(6) Type I schizophrenia is seen as "positive symptoms"; eg: hallucinations and delusions, and type II as "negative symptoms", like inactivity and flatness of emotions (Brewer 2001).

(7) Features include in mild forms: headaches and vomiting; in moderate form: muscle cramps and weakness; in severe form: drowsiness and diminished reflexes (Baylis 1996).

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